Cervical Cancer in Ontario 1971-1996

Preface/Executive Summary /Background

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Preface

This monograph on cervical cancer in Ontario was developed to provide comprehensive background information for the Ontario Cervical Screening Program (OCSP) and as a resource document for planning.

The basis for the information in this monograph is the Ontario Cancer Registry (OCR). Both the OCSP and the OCR are operated by Cancer Care Ontario (CCO), through funding by the Ontario Ministry of Health. The OCSP and the OCR are situated within the Screening Unit and the Surveillance Unit, respectively, of the Division of Preventive Oncology, which is located at the Provincial Office of CCO in Toronto.

The authors would like to thank Dr. Philippa Holowaty for providing hysterectomy prevalence rates, Dr. Barry Rosen for contributing to the clinical sections in the background (Signs and symptoms, Diagnosis and staging, Treatment and Prognosis), Drs. Patricia Shaw and Meg McLachlin, members of the Ontario Cervical Screening Collaborative Group, for their advice regarding morphologic groupings, and Mr. Robert Semenciw for providing age-standardized incidence rates of cervical cancer by province. We are also grateful to Dr. Richard Schabas, Head of the Division of Preventive Oncology, Dr. Eric Holowaty, Director of the Surveillance Unit, and Dr. Verna Mai, Director of the Screening Unit, for reviewing a draft of this document.

This monograph could not have been produced without the valuable assistance of Mrs. Virginia Hunter (desktop publishing), and Ms. Vicky Majpruz-Moat and Ms. Sandrene Chin Cheong (technical support and graphics). Finally, the authors would like to acknowledge the contribution of all the operations staff within the Surveillance Unit and the Registry Support Group (within the Information Systems Department), for their ongoing efforts in ensuring the generation of timely and high-quality cancer incidence data for Ontario.

Executive Summary

Although cervical cancer is relatively uncommon in Ontario females (ranking eighth in terms of incidence and eleventh in terms of cancer causes of death), it is among the most important cancers in young women, ranking third in incidence among those aged 20-34 and second among those aged 35-49. There is considerable geographic variation in the incidence of this cancer within Ontario, across Canada and particularly around the world: there was a greater than 10-fold difference in incidence rates between low incidence areas (such as Finland and China) and high ones (such as Latin America and South East Asia). Ontario's annual incidence is intermediate. It was 9.9 per 100,000 women in 1994-1996 (age-standardized to the Canadian 1991 population). When corrected for the estimated number of women who have had a hysterectomy and are therefore not at risk of getting cervical cancer, the incidence was 12.6 per 100,000.

The incidence of cervical cancer in Ontario has decreased by about 46% since 1971, the earliest year for which reliable statistics are available from the Ontario Cancer Registry. The drop was greatest in younger women (those aged 20-34 and 35-49). However, despite striking declines in incidence in the 1970s (8-10% per year in younger women), recent gains have been much more modest (0.8-1.6% decreases per year in all age groups since the early 1980s). Mortality also decreased by 46% over the 26-year period.

Incidence trends differed dramatically according to the morphologic type of the cervical cancer, with declines restricted to invasive squamous cell carcinoma. Incidence of the other major morphologic types, adenocarcinoma and adenosquamous carcinoma, increased by 5.8% per year in women under the age of 50 years.

Five-year relative survival for cervical cancer in Ontario was 70.3%, and did not vary with year of diagnosis. It did, however, differ across age groups, ranging from a high of 83.9% among women diagnosed at ages 20-34 to a low of 50.9% for those diagnosed at age 65 years or over. Relative survival was the same for invasive squamous cell carcinoma as for adenocarcinoma and adenosquamous carcinoma combined.

Cervical cancer is largely preventable through appropriate utilization of Pap test screening. The substantial declines in incidence and mortality in Ontario during the 1970s and, in some age groups, into the 1980s were likely due in large part to the increased use of the Pap test through the 1960s and later. However, the slowing of the downward trend in the incidence of invasive squamous cell carcinoma in the 1980s and onwards, combined with the increasing incidence of cervical adenocarcinoma and adenosquamous carcinoma, suggests that the gains obtainable through "opportunistic" screening in Ontario may have been maximized, and that a more organized approach to Pap test screening is required to further reduce the incidence of this disease. An alternative explanation is that the increasing incidence of adenocarcinoma is indicative of what the trends for squamous cell carcinoma would be in the absence of screening. Under this scenario, the slowing of the downward trend may be due to the opposing forces of static screening and a true increase in incidence.

Pap test screening is most effective at preventing the development of invasive squamous cell carcinoma, through detection and effective treatment of its precursors. Other morphologic types are not as effectively prevented by use of Pap test screening as historically practised in Ontario.

Assuming that invasive squamous cell carcinoma could be completely prevented if a high-quality cervical cancer screening program were in place, it should be possible to lower the overall incidence of cervical cancer in Ontario from 9.9 per 100,000 (1994-1996 incidence, uncorrected for hysterectomy) to 4.5 per 100,000 (by removing the 5.4 per 100,000 women diagnosed with invasive squamous cell carcinoma); this is a drop of 54%. While this represents the maximum potential gain in terms of squamous cell carcinoma in the long run, smaller but substantial gains could be had more immediately by improving the coverage and effectiveness of cervical cancer screening in Ontario.

More than half the residual rate of cervical cancer (i.e. half of 4.5 per 100,000) would be comprised of adenocarcinoma and adenosquamous carcinoma. If increases in the incidence of these types continue, then the gains from screening will appear to be less. However, if recently recommended techniques for taking Pap tests (i.e. using the brush as well as spatula) are widely adopted in Ontario, it may be possible to reduce the incidence of these forms of cervical cancer as well. The magnitude of such reductions cannot be predicted at this time.

Background

Introduction

Cancer of the uterine cervix was diagnosed in an estimated 560 Ontario women in 1998, based on projected incidence, and an estimated 150 women died from it (National Cancer Institute of Canada 1998). Over a lifetime, this potentially preventable cancer will affect about 1 in 122 women, based on current Canadian incidence rates (Table 1). Although only the eighth most common cancer in Ontario women of all ages, among younger women it ranks second (ages 35-49) or third (ages 20-34).

Table 1. Probability[1] of developing cervical cancer in Canada, by age (NCIC 1998)

	Cumulative probability[1] (%) of developing cervical cancer by age:							Lifetime probability	
Age	30	40	50	60	70	80	90	%	One in:
Probability	0.1	0.2	0.3	0.5	0.6	0.7	0.8	0.8	122.0

[1] The probability of developing cervical cancer is based on age-specific cancer incidence rates for Canada in 1993 and on life tables based on 1992-1994 all-cause mortality rates

Decreasing trends in incidence and mortality rates in Ontario and elsewhere have been widely attributed to screening with Papanicolau (Pap) tests. This procedure, introduced in Ontario during the 1960s, collects cervical cells for microscopic examination to detect both cervical cancer and the precursor lesions called cervical intraepithelial neoplasia or dysplasia. While most cervical dysplasias regress, a proportion progress to cancer (Holowaty et al. 1999).

Anatomy

The cervix is the cylindrically shaped lower third of the uterus extending into the vagina (Figure 1). The part of the cervix that projects into the vagina (the ectocervix) is covered by squamous cells similar to the neighbouring lining of the vagina (Figure 2). The endocervical canal is covered by mucus-secreting columnar cells related to those lining the uterus. The junction between these two types of cells, squamous and columnar, is called the transformation zone, and is the area where benign and malignant changes are most likely to occur. With age, this area moves up into the endocervical canal.

Figure 1. Female reproductive system

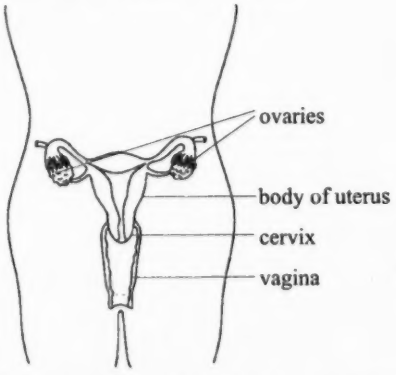
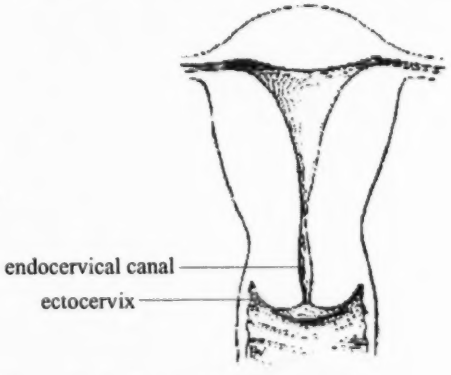


Figure 2. Uterus showing parts of the cervix



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Malignancies of the uterine cervix

Squamous cell carcinoma accounts for most cervical cancers. Adenocarcinoma, arising in the cells of the endocervical canal, is the second most common morphologic type. Adenosquamous carcinoma, as the name suggests, shares some features of both major types. Other morphologic types, such as sarcoma, rarely occur in the cervix.

Decreasing rates for all cervical cancer diagnoses and deaths over time mask a concurrent increase in adenocarcinoma in several populations (Zheng et al. 1996; Vizcaino et al. 1998). The increasing incidence of adenocarcinoma of the cervix may be partly attributable to an increasing prevalence of human papillomavirus infection (HPV) (Zheng et al. 1996; Vizcaino et al. 1998). Rising incidence of adenocarcinoma has paralleled a rise in the incidence of genital warts, which are also caused by HPV (Kjaer and Brinton 1993). Another possible explanation for the increasing incidence of adenocarcinoma is improvements in screening. There has been increasing recognition of both the need to capture cells for Pap tests from higher in the endocervical canal, where adenocarcinoma arises, and the difficulty of interpreting changes in endocervical cells (Luzzatto and Boon 1996; Nieminen et al. 1995; Lee et al. 1997; Bose et al. 1994).

Risk factors

Human papillomavirus infection (in particular, persistent infection with types 16 and 18) is the primary risk factor for cervical cancer (Bosch et al. 1995; Schiffman and Brinton 1995). This may explain the many findings of positive association between this cancer and early age at first marriage, early age at first pregnancy, more children, early age at first intercourse, and greater number of sexual partners (or spouse's sexual partners). Since HPV infection is widely prevalent, a variety of cofactors and molecular events must presumably occur between HPV infection and development of cervical cancer or its precursors (Richart et al. 1998; Schiffman and Brinton 1995). Cigarette smoking appears to be a major cofactor (Ho et al. 1998; Olsen et al. 1998). Oral contraceptive use is associated with both squamous cell carcinoma and adenocarcinoma (Beral et al. 1999; Thomas and Ray 1996; Ursin et al. 1996). Deficient nutrition may affect the risk of persistent infection, lesion development, or both (Villa 1997; Giuliano et al. 1997; Potischman and Brinton 1996).

Cervical cancer occurs more frequently in women of low socioeconomic status and in immigrant and aboriginal women. In addition to some differences in risk factor levels, this may reflect underscreening resulting from competing and more immediate health and survival issues, and limited access to nonthreatening, culturally sensitive preventive care.

Prevention and early detection

Carcinoma of the cervix can be prevented by the early detection of cancerous or precancerous lesions using the Pap test. Table 2 shows Ontario women's self-reports of Pap tests for the regions reported by the 1996-1997 National Population Health Survey. (Self-reports may overestimate testing, or report tests more recently than they occurred (Bowman et al. 1997; Walter et al. 1988).) High percentages of women in Toronto and Peel regions reporting that they have never had a Pap test probably reflects, among other things, high immigrant populations in these areas.

Table 2. Pap test histories reported by Ontario women aged 20 and over, by region, 1996-1997

National Population Health Survey (NPHS) Region[1]	Time since last Pap test (%)[2] 0-3 years	3+ years	Never had a Pap test (%)[2]
Algoma, Cochrane	70.5	20.6	8.9
Brant, Haldimand-Norfolk	73.9	16.7	9.4
Bruce, Grey, Perth, Huron	73.8	17.5	8.7
Durham	75.4	16.2	8.3
Elgin, Middlesex, Oxford	71.0	19.9	9.1
Essex	71.3	18.5	10.2
Halton	77.1	13.6	9.3
Hamilton-Wentworth	70.2	17.4	12.4
Lambton, Kent	75.1	18.1	6.8
Lanark, Leeds & Grenville, Hastings, Prince Edward, Frontenac, Lennox & Addington	74.2	17.9	7.9
Manitoulin Island, Sudbury District, Sudbury R.M.	72.3	20.0	7.7
Niagara	67.1	24.2	8.7
Northumberland, Victoria, Haliburton, Peterborough	73.3	20.1	6.6
Ottawa-Carleton	79.9	12.4	7.7
Peel	73.2	12.7	14.1
Prescott & Russell, Stormont-Dundas & Glengarry, Renfrew	74.7	16.7	8.6
Simcoe	77.1	16.4	6.4
Thunder Bay, Kenora, Rainy River	76.7	17.8	5.6
Timiskaming, Muskoka, Parry Sound, Nipissing	75.1	17.7	7.2
Toronto	71.5	10.3	18.2
Waterloo	74.3	17.1	8.6
Wellington, Dufferin	75.0	16.1	8.9
York	78.9	11.7	9.5
All Ontario	**74.1**	**14.8**	**11.0**

[1] Regions are agglomerations of census divisions

[2] Age-standardized to the Ontario NPHS population of women aged 20 and over

In Ontario, as in the rest of Canada and much of the developed world, many women continue to have annual Pap tests year after year while others are never or seldom screened, or cease screening after their childbearing years (Lee et al. 1998). The Ontario Cervical Screening Collaborative Group recommends screening sexually active or formerly active women of all ages every two years (after three annual normal tests). It also recommends that screening be discontinued after age 70 for women with four normal tests in the previous ten years. Its guidelines encourage the use of a brush or similar sampling device that captures cells from the endocervical canal, in addition to a spatula. The Group

is working to reduce incidence and mortality rates by improving the effectiveness of cervical screening in Ontario, including strategies to extend this cancer prevention measure to women currently unscreened or underscreened (Ontario Cervical Screening Collaborative Group 1996).

HPV detection and typing, and development of an HPV vaccine, may become practical measures for cervical cancer prevention in the future (Villa 1997; Arends et al. 1998). For the time being, improving the existing Pap test screening system is the best means of lowering the incidence of this largely preventable cancer.

Signs and symptoms

Cancers detected by Pap tests are usually asymptomatic. The rest are diagnosed through investigation of symptoms, of which the most common are abnormal vaginal bleeding or discharge. Bleeding can be spontaneous and irregular, or postcoital (following intercourse). The presenting symptom may be pain resulting from spread to either surrounding tissues or regional lymph nodes; very rarely, it is costovertebral tenderness secondary to ureteric obstruction or a cough secondary to lung metastasis.

Diagnosis and staging

A woman with an abnormal Pap test is usually referred for colposcopy, where under direct magnified vision a biopsy of the abnormal area on the cervix can be taken. If presenting with bleeding, she will initially have a Pap test and a biopsy of any lesion or abnormal area seen on colposcopy. The biopsied tissue is then examined microscopically and the histological diagnosis made.

Once diagnosed, the cancer is staged (that is, the extent of spread is investigated) so that appropriate treatment can be initiated. Staging is based on a physical examination, sometimes under anaesthesia, to determine whether the cancer is limited to the cervix or has spread into the parametrium (connective tissue surrounding the uterus) or into the vagina. Chest x-ray, IVP, cystoscopy, and sigmoidoscopy are sometimes used in addition to physical examination. (MRI and CT scans are often used to help in planning treatment.) Tumours limited to the cervix are designated Stage I. Stage II describes tumours that have spread into the parametrium (but not all the way to the pelvic side wall); it includes spread to the proximal vagina. Stage III tumours have spread into the pelvic side wall or the lower third of the vagina. Stage IV includes distant spread or tumour invading the bladder or rectal mucosa.

Treatment

Treatment includes surgery, radiation or a combination of the two. Surgery alone is reserved for the otherwise well woman with a Stage I tumour less than 4 centimeters (cm) in size. Surgery for these smaller Stage I tumours includes a radical hysterectomy and bilateral pelvic node dissection. In younger women, the ovaries are not removed, thus allowing for the benefits of endogenous hormone production. When tumour size is 4 cm or greater, the chance of lymph node metastasis is greatly increased (Finan et al. 1996; Fuller et al. 1989). In this situation, radiation therapy provides better control of the tumour. When tumour pathology demonstrates poor prognostic factors (depth of invasion > 50%, capillary-like space involvement, close or involved margins) pelvic radiation therapy is added to the surgery.

Stage I tumours greater than 4 cm and Stage II and III tumours are treated primarily with pelvic radiation, either intracavitary or external beam. When there is evidence of spread to lymph nodes in

the common iliac or higher nodal chain, extended field radiation may be used; this includes treatment to the para-aortic regions. Treatment for women with Stage IV cervical cancer is usually individualized to the situation. It may include chemotherapy for lung metastasis, or palliative surgery for a vesicovaginal or rectovaginal fistula. Five recent randomized clinical trials demonstrate that adding platinum-based chemotherapy to radiotherapy prolongs survival in women with locally advanced cervical cancer (Stages IB-IVA), as well as those with Stage I-IIA disease and metastases to pelvic lymph nodes, parametrial disease, or positive surgical margins (National Cancer Institute 1999).

To investigate actual Ontario care patterns, a cohort of all women diagnosed with cervical cancer of squamous cell, adenosquamous, or certain non-specific morphologies between 1993 and 1994 was identified from the Ontario Cancer Registry (OCR) (n=874). All OCR records (hospital discharges, same day surgery records, pathology reports, and reports of visits to the regional cancer centres of Cancer Care Ontario or Princess Margaret Hospital) for the 12 months following diagnosis were identified for the cohort. Treatment data were extracted from these records (surgical procedures, radiation therapy or outpatient procedures). No data were available for stage of disease in this cohort.

Table 3 shows the distribution of treatments received during the first year after diagnosis. Three hundred and thirty-two (332) women (38% of the cohort) had some form of hysterectomy and 350 women (40%) had either external beam radiation or brachytherapy (including 64 women (7.3%) who had both surgery and radiation). The remaining 256 women (29.3%) had unspecified treatment or local treatment only (local excision of the cancer), either as a hospital in- or outpatient or in a physician's office or clinic.

Table 3. Treatment received within 12 months of diagnosis of cervical cancer,[1] Ontario, 1993-1994

Treatment	Number of women[2] (%)
Hysterectomy	332 (38.0)
Radiotherapy	350 (40.0)
Local and unspecified treatment	256 (29.3)

[1] Includes all cases with ICD-9 code 180 and ICD-O morphology 804-808 (squamous cell); 856, 857 (adenosquamous and adenocarcinoma with squamous metaplasia); 800-802, 999 (carcinoma not otherwise specified and unspecified histology)

[2] Percentages are of 874. Numbers do not add to 874 because 64 women had both hysterectomy and radiotherapy

Prognosis

Prognosis is closely linked to stage: Stage I has the best outcome and Stage IV the worst (Barillot et al. 1997; Perez et al. 1998). Within Stage I, smaller tumours have a better outcome and there is a direct relationship between size and risk of nodal spread (Fuller et al. 1989; Eifel et al. 1994; Finan et al. 1996). When disease has spread to regional lymph nodes survival is greatly reduced (Yuan et al. 1998; Yeh et al. 1999; Barillot et al. 1997).

Morphology may also convey prognostic information. Although some studies show differences in outcome between adenocarcinoma and squamous cell carcinoma, most large or population-based studies show no survival differences (Anton-Culver et al. 1992; Hopkins and Morley 1991; Shingleton et al. 1995). Some of the rare morphologies such as clear cell, glassy cell and small cell (neuroendocrine) carcinoma have a poorer prognosis than squamous cell cancer (Benda 1994). Tumour grade (the degree to which cells do not resemble normal tissue) has also been associated with outcome: grade I tumours have a better outcome than grade III tumours. Other factors affecting outcome include whether or not there is capillary-lymphatic space invasion, and whether the tumour has deeply invaded (> 50%) the cervix in Stage I tumours (Eifel et al. 1997; Yuan et al. 1998; Benda 1996).

Cervical Cancer in Ontario 1971-1996

Incidence and Mortality

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Most common cancers and cancer causes of death

The Ontario Cancer Registry (OCR) recorded 105,901 cancers newly diagnosed in Ontario females in 1992-1996. Although the cervix was a relatively uncommon site of cancer in females of all ages, ranking eighth (2,897 cases, 2.7%) (Table 4), it was one of the more common sites among women 20 to 49 years of age (Table 5). Cervical cancer was the second most common cancer for women 35 to 49 years of age (after cancer of the breast) and ranked third for women 20 to 34 years of age (after cancers of the breast and thyroid).

Cancer was the cause of death for 48,937 Ontario females in the 5-year period 1992 to 1996. Cervical cancer was relatively rare as a cancer cause of death, ranking eleventh for all females (821 deaths, 1.7%).

Table 4. Most common cancers diagnosed in Ontario females,[1] 1992-1996

		Cancer cases	
Rank	**Site**	**#**	**%**
1	Breast	30,334	28.6
2	Colon/rectum	13,686	12.9
3	Lung	12,149	11.5
4	Corpus uteri	5,751	5.4
5	Ovary	4,553	4.3
6	Non-Hodgkin's lymphoma	4,078	3.9
7	Melanoma	2,985	2.8
8	Cervix	2,897	2.7
9	Leukemia	2,827	2.7
10	Pancreas	2,588	2.4
	All other sites	24,053	22.7

[1] Non- melanoma skin cancer is not included as it is not recorded in the OCR

Table 5. Ranking of cervical cancer relative to other cancers in Ontario women, by age group, 1992-1996

Age group	Rank	#	%[1]
20-34	3	521	12.6
35-49	2	1,118	7.1
50-64	9	595	2.1
65+	16	659	1.1

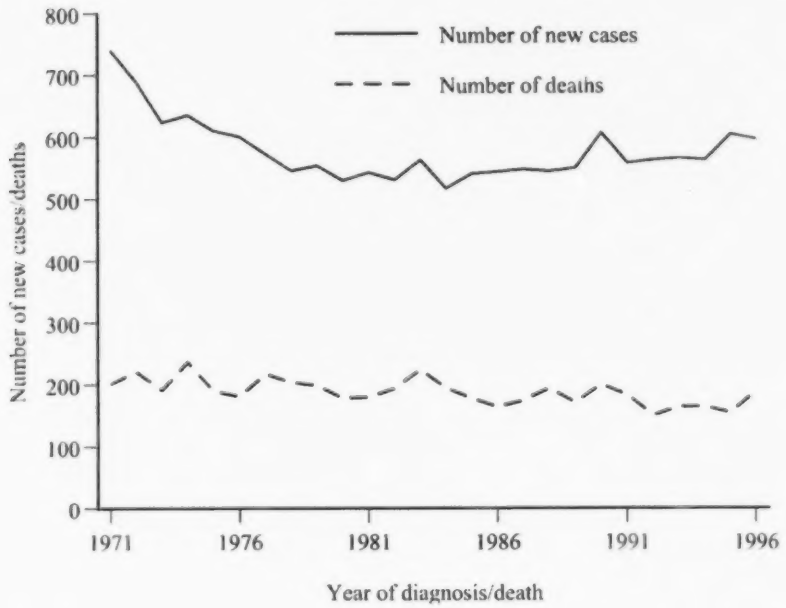
[1] Percentage of all cancers in the age group

Numbers of new cases and deaths

The number of new cases of cervical cancer diagnosed annually in Ontario decreased from 741 to 517 (30% decrease) between 1971 and 1984 (Figure 3). Since then, the annual number has increased slightly from 541 in 1985 to 596 in 1996.

The numbers of deaths were smaller than the numbers of new cases and have remained relatively stable over time. There were 202 cervical cancer deaths in 1971 and 189 in 1996.

Figure 3. Numbers of new cases of and deaths from cervical cancer in Ontario, by year, 1971-1996

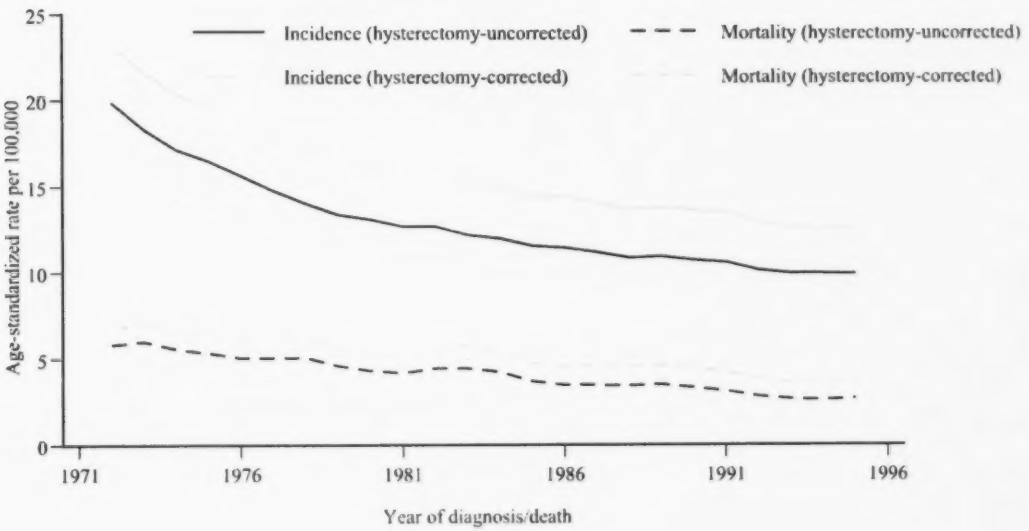


Trends in incidence and mortality

Age-standardized incidence and mortality rates for cervical cancer (using both uncorrected and hysterectomy-corrected populations) are shown in Figure 4 for the time period 1971-1996. (Rates are age-standardized to the 1991 Canadian population, Appendix A.) Incidence rates declined continuously, from 23.2 per 100,000 (hysterectomy-corrected) in 1971-1973 to 12.6 per 100,000 in 1994-1996, a decrease of 46%. This decline was steeper from 1971-1979 (an annual percentage change of 5.4%) than from 1980 to 1996 (an annual percentage change of 1.3%).

Mortality rates showed a fairly similar pattern, declining continuously from 6.8 per 100,000 (hysterectomy-corrected) in 1971-1973 to 3.7 per 100,000 in 1994-1996 (a 46% decrease). This represents an annual percentage decrease of 2.9%, which was constant over the time period.

Figure 4. Age-standardized incidence and mortality rates (3-year moving averages) for cervical cancer in Ontario, by year, 1971-1996

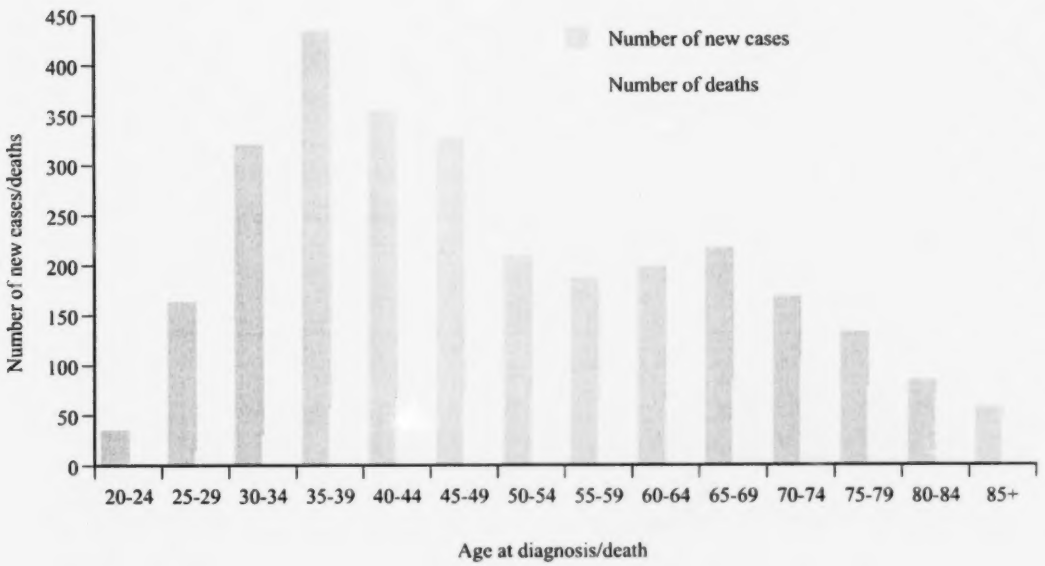


Numbers of new cases and deaths, by age

Cervical cancers occurred rarely prior to the age of 20. After age 20, the number of newly diagnosed cases increased with age to a peak in the 35-39 age group where 434 females were diagnosed with cervical cancer during the 5-year period 1992-1996 (Figure 5). Overall, the numbers of cases were highest in women from age 30 to age 49.

The numbers of cervical cancer deaths increased steadily with age to a peak in the 70-74 age group, where 103 females died of cervical cancer in 1992-1996. The numbers of deaths were considerably less than the numbers of new cases in every age group, except for women 80 years of age or older. For these women, the number of deaths (118) was only slightly smaller than the number of new cases (141).

Figure 5. Numbers of new cases of and deaths from cervical cancer in Ontario, by age group, 1992-1996

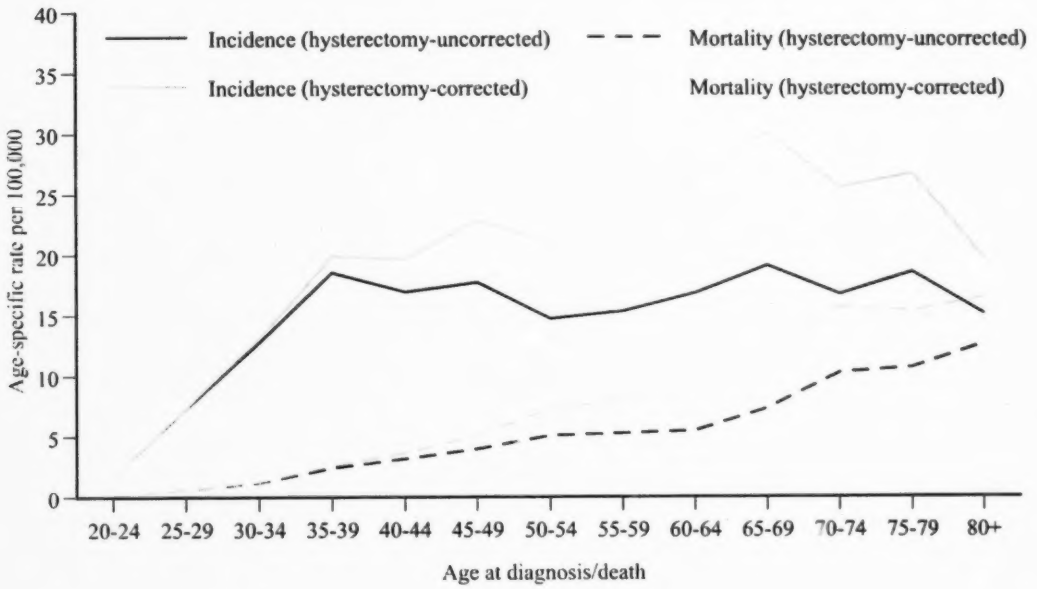


Age-specific incidence and mortality

Figure 6 shows the age-specific incidence and mortality rates for the time period 1992-1996, using both uncorrected and hysterectomy-corrected populations. Incidence rates (corrected for hysterectomy) increased with age to a peak in the 65-69 age group, where the incidence was 30.1 per 100,000 women per year. Incidence declined with age thereafter.

Age-specific mortality rates increased steadily with age, reaching 16.5 per 100,000 women per year for those aged 80+. In contrast to incidence, there was no drop at the older ages for mortality.

Figure 6. Age-specific incidence and mortality rates in Ontario, by age group, 1992-1996



Trends in incidence, by age group

Figure 7 shows hysterectomy-corrected incidence rates according to age at diagnosis, for the time period 1971-1996. Incidence was lowest for those aged 20-34 and highest for those aged 50-64 and 65+.

For every age group, the rate of decrease was greater during the earlier part of the time period (Table 6). For example, in women aged 20-34, hysterectomy-corrected incidence rates declined by 8.3% per year between 1971 and 1974 and by only 0.9% per year thereafter. Early annual decreases were greatest in the two youngest age groups (8.3% for ages 20-34 and 9.7% for ages 35-49), while declines in more recent years were fairly similar across age groups (0.8%-1.6% per year).

Figure 7. Age-standardized hysterectomy-corrected incidence rates (3-year moving averages) for cervical cancer in Ontario, by age group, 1971-1996

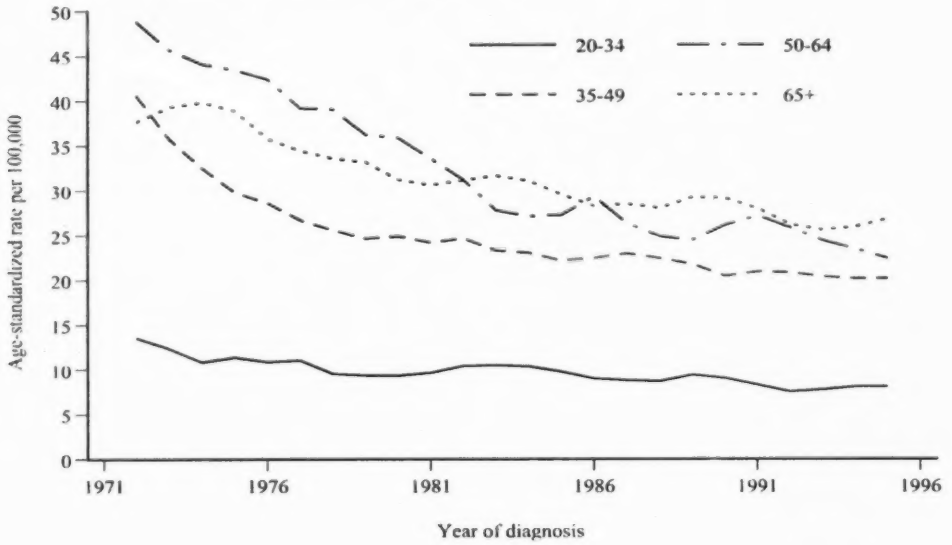


Table 6. Annual percentage change (APC) for cervical cancer incidence (hysterectomy-corrected) in Ontario, by age group, 1971-1996

Age group	Period	APC (%)
20-34	1971-1974	-8.3
	1975-1996	-0.9
35-49	1971-1976	-9.7
	1977-1996	-1.4
50-64	1971-1982	-4.3
	1983-1996	-1.6
65+	1971-1984	-2.3
	1985-1996	-0.8

Trends in mortality, by age group

Figure 8 shows hysterectomy-corrected mortality rates according to age at death for the time period 1971-1996. Mortality was lowest for those aged 20-34 and highest for those aged 65+.

Mortality rates decreased over time for every age group except 20-34 (Table 7). Decreases were greatest in those aged 35-49 and 50-64, where rates declined by an average of 3.8% and 3.3% per year, respectively. Mortality remained stable in the youngest women (age 20-34), although the small numbers of deaths in this age group produce relatively unstable rates. In the oldest age group (65+), mortality did not start to decline significantly until 1984; rates decreased by 1.9% per year thereafter.

Figure 8. Age-standardized hysterectomy-corrected mortality rates (3-year moving averages) for cervical cancer in Ontario, by age group, 1971-1996

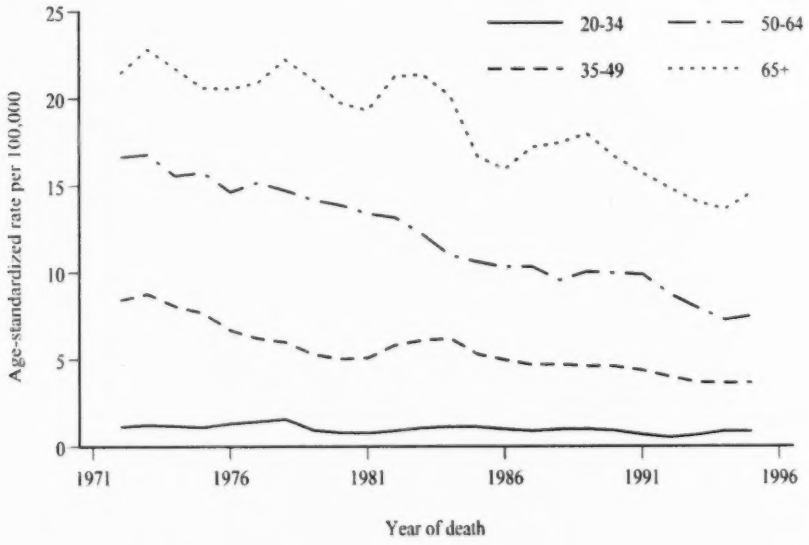


Table 7. Annual percentage change (APC) for cervical cancer mortality (hysterectomy-corrected) in Ontario, by age group, 1971-1996

Age group	Period	APC (%)
20-34	1971-1996	0.0
35-49	1971-1996	-3.8
50-64	1971-1996	-3.3
65+	1971-1983	0.0
	1984-1996	-1.9

Cervical Cancer in Ontario 1971-1996

Geographic Patterns

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Intraprovincial comparisons

Age-standardized incidence rates for 1992-1996 (uncorrected for hysterectomy) ranged from 8.6 and 8.7 per 100,000 in the Eastern and Southwest Cancer Care Ontario Regions (CCORs), respectively, to 12.3 in the Northeast CCOR, a 43% difference (Table 8). The incidence rate ratio significantly exceeded 1.0 (i.e. the rate in the CCOR was significantly greater than that for all Ontario combined) in the Northeast. The Eastern and Southwest CCORs had incidence rates that were significantly lower than the all-Ontario rate. (Definitions of the CCORs are found in Appendix B.)

Mortality showed a similar pattern (Table 8): a significantly higher rate in the Northeast CCOR and a significantly lower rate in the Southwest CCOR. Although the Northwest CCOR had the highest mortality rate, it was not significantly higher than that for all Ontario, presumably because the number of deaths in this region was very small.

Table 9 and Figure 9 present the age-standardized incidence rates for the province's 37 Public Health Units (PHUs) for the time period 1992-1996, (uncorrected for hysterectomy). (Definitions of the PHUs are found in Appendix C.) Since many of these rates are based on very small numbers of cases of cervical cancer, they should be interpreted with caution. Incidence ranged from a high of 16.9 per 100,000 in Timiskaming to a low of 6.4 in Elgin-St. Thomas. Several PHUs had rates which were significantly higher than the provincial average, including Haliburton-Kawartha-Pine Ridge, Muskoka-Parry Sound, Porcupine, Simcoe and Timiskaming. A number of these PHUs are located in the Northeast CCOR. The Hamilton-Wentworth and Ottawa-Carleton PHUs had significantly low incidence rates of cervical cancer.

Table 8. Age-standardized[1] incidence and mortality rates[2] (per 100,000), rate ratios[3] (RR) and 95% confidence intervals (CI) for cervical cancer, by CCOR, 1992-1996

	Incidence				Mortality			
CCOR	**#**	**Rate**	**RR**	**95% CI**	**#**	**Rate**	**RR**	**95% CI**
Eastern	254	8.6	0.88*	(0.77, 0.99)	75	2.4	0.91	(0.72, 1.14)
Southeast	181	10.5	1.08	(0.93, 1.25)	63	3.3	1.25	(0.97, 1.60)
Central East	1,381	10.2	1.04	(0.99, 1.10)	379	2.7	1.02	(0.92, 1.13)
Central West	322	9.0	0.92	(0.82, 1.03)	92	2.3	0.86	(0.69, 1.05)
Southwest	350	8.7	0.90*	(0.80, 0.99)	94	2.1	0.80*	(0.65, 0.97)
South	88	9.6	0.99	(0.79, 1.21)	24	2.3	0.88	(0.57, 1.31)
Northeast	194	12.3	1.26*	(1.09, 1.44)	65	3.8	1.43*	(1.11, 1.82)
Northwest	67	10.6	1.08	(0.85, 1.37)	26	3.9	1.46	(0.97, 2.12)
All Ontario[4]	**2,837**	**9.8**	**1.00**		**818**	**2.7**	**1.00**	

[1] Standardized to the 1991 Canadian population

[2] Uncorrected for hysterectomy

[3] Ratio of the incidence or mortality rate in a CCOR to that for all Ontario (known residence only)

[4] Excludes cases and deaths with unknown residence

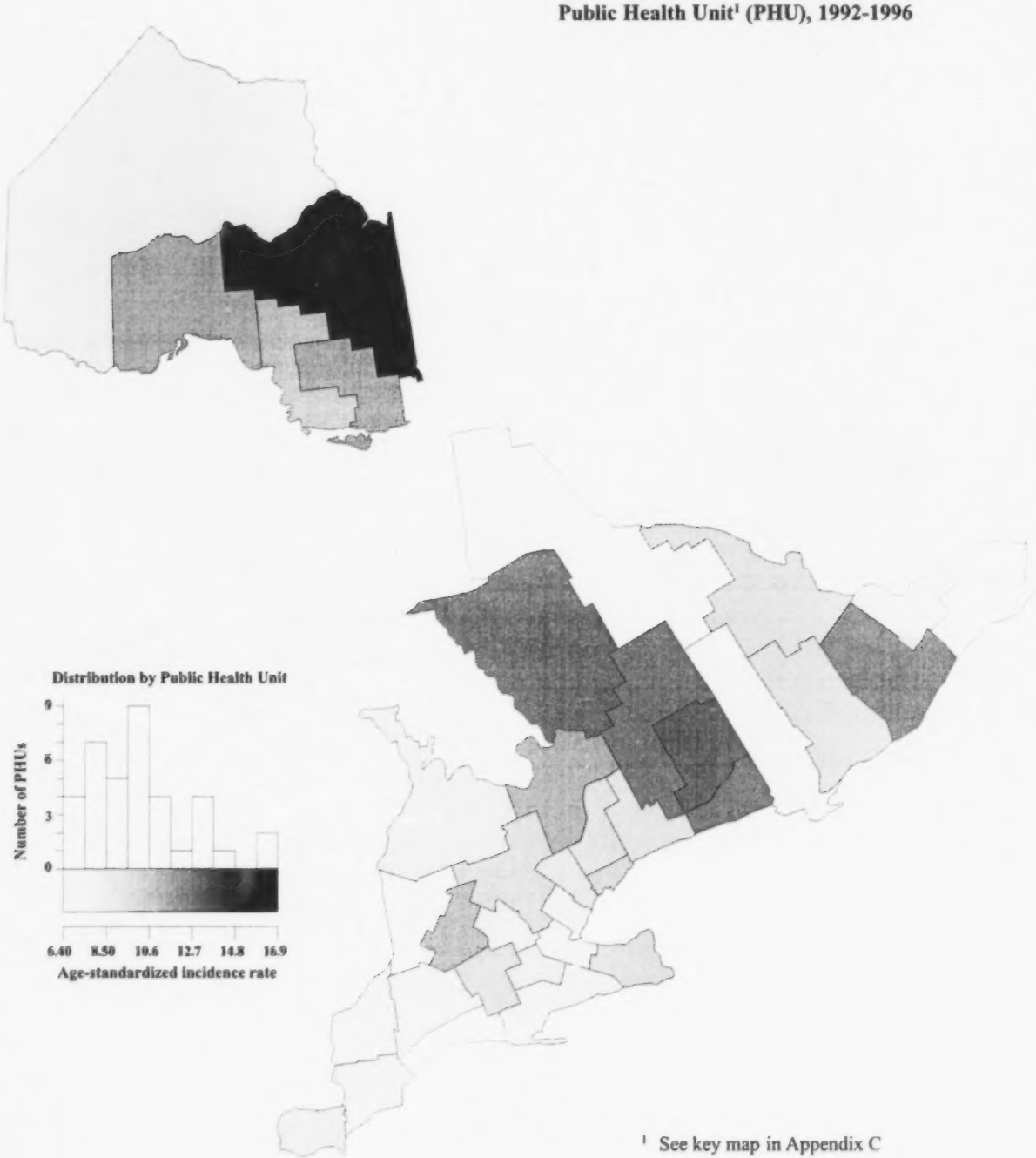
* Significantly different from 1.0 ($p<0.05$)

Table 9. Age-standardized[1] incidence rates[2] (per 100,000), rate ratios[3] (RR) and 95% confidence intervals (CI) for cervical cancer, by Public Health Unit, 1992-1996

		Incidence		
Public Health Unit	**#**	**Rate**	**RR**	**95% CI**
Algoma	39	11.1	1.14	(0.82, 1.55)
Brant	30	9.3	0.95	(0.65, 1.34)
Bruce-Grey-Owen Sound	39	9.4	0.96	(0.69, 1.32)
Durham	109	9.7	0.99	(0.82, 1.19)
Eastern Ontario	40	7.6	0.78	(0.56, 1.05)
Elgin-St. Thomas	14	6.4	0.66	(0.37, 1.09)
Haldimand-Norfolk	22	8.2	0.84	(0.54, 1.27)
Haliburton-Kawartha-Pine Ridge	60	12.9	1.32*	(1.00, 1.70)
Halton	76	8.3	0.85	(0.67, 1.06)
Hamilton-Wentworth	100	7.9	0.81*	(0.66, 0.98)
Hastings-Prince Edward	28	7.0	0.72	(0.48, 1.03)
Huron	12	7.2	0.74	(0.39, 1.31)
Kent-Chatham	25	8.7	0.89	(0.58, 1.30)
Kingston-Frontenac-Lennox-Addington	48	10.0	1.02	(0.76, 1.35)
Lambton	30	8.4	0.86	(0.59, 1.21)
Leeds-Grenville-Lanark	54	12.8	1.31	(0.99, 1.70)
Middlesex-London	88	8.1	0.83	(0.67, 1.02)
Muskoka-Parry Sound	38	14.5	1.49*	(1.05, 2.06)
Niagara	114	9.8	1.00	(0.83, 1.21)
North Bay and District	16	6.5	0.67	(0.39, 1.07)
Northwestern	18	8.6	0.88	(0.54, 1.37)
Ottawa-Carleton	168	8.3	0.85*	(0.73, 0.99)
Oxford	28	11.3	1.16	(0.78, 1.67)
Peel	203	9.7	1.00	(0.87, 1.15)
Perth	21	11.6	1.19	(0.75, 1.80)
Peterborough	45	13.0	1.33	(0.97, 1.78)
Porcupine	37	16.0	1.63*	(1.17, 2.23)
Renfrew	25	9.9	1.02	(0.67, 1.49)
Simcoe	109	12.7	1.30*	(1.07, 1.56)
Sudbury and District	65	12.0	1.23	(0.95, 1.55)
Thunder Bay	49	11.5	1.18	(0.88, 1.55)
Timiskaming	17	16.9	1.73*	(1.03, 2.77)
Toronto	692	10.2	1.05	(0.97, 1.13)
Waterloo	93	8.9	0.91	(0.74, 1.12)
Wellington-Dufferin-Guelph	56	10.1	1.03	(0.79, 1.33)
Windsor-Essex	88	9.6	0.99	(0.79, 1.21)
York	141	9.8	1.00	(0.84, 1.18)
All Ontario[4]	**2,837**	**9.8**	**1.00**	

[1] Standardized to the 1991 Canadian population
[2] Uncorrected for hysterectomy
[3] Ratio of the incidence rate in a Public Health Unit to that for all Ontario (known residence only)
[4] Excludes cases with unknown residence
* Significantly different from 1.0 ($p<0.05$)

Figure 9. Age-standardized incidence rates (per 100,000) for cervical cancer, by Public Health Unit[1] (PHU), 1992-1996



[1] See key map in Appendix C

Interprovincial comparisons

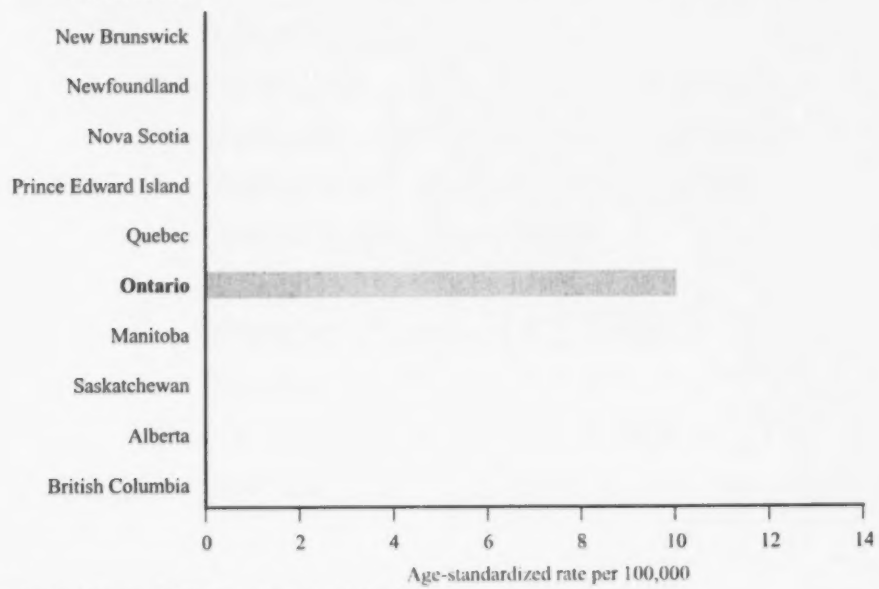
Figure 10 compares the incidence of cervical cancer (uncorrected for hysterectomy) in Ontario with that in the other provinces of Canada in 1991-1995, the most recent available years of data (Quebec data cover only 1991-1994). Incidence was generally highest in the east (between 11.4 and 12.4 per 100,000 in Nova Scotia, Newfoundland, and Prince Edward Island) and lowest in New Brunswick, Quebec (for which there are concerns about the completeness of cancer registration), Saskatchewan and British Columbia (between 8.2 and 8.8 per 100,000). The other provinces, including Ontario, had intermediate rates (10 per 100,000).

Possible explanations for this variation include differences in Pap test screening coverage, degree of organization of Pap test screening efforts, and hysterectomy prevalence rates.

The proportion of women who reported in 1994-1995 that they had had a Pap test within the preceding three years ranged from a high of 74% in the prairie provinces to a low of 62.5% in Quebec (Snider and Beauvais 1998); screening rates were very similar in the other three regions (67.2%-68.6%). Further, some provinces, such as British Columbia, have had components of organized Pap test screening in place for decades, while other provinces, such as Ontario and Alberta, have only recently begun to develop more organized screening.

While hysterectomy prevalence varies considerably by region (Snider and Beauvais 1998), it is unlikely to account for the variation in incidence: the region with the highest cancer rate, Atlantic Canada, has the highest reported hysterectomy prevalence, while areas with the lowest cervical cancer rates have the lowest hysterectomy prevalence rates.

Figure 10. Age-standardized[1] incidence rates[2] for cervical cancer, by province of Canada, 1991-1995[3]



[1] Standardized to the 1991 Canadian population

[2] Uncorrected for hysterectomy

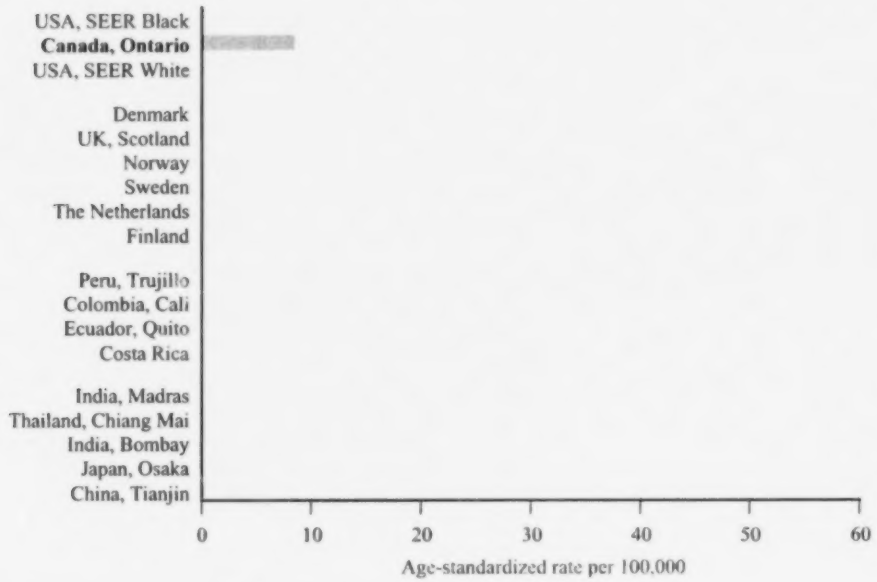
[3] For Quebec, data are for 1991-1994

International comparisons

There was considerably more variation in cervical cancer incidence internationally (Figure 11) than either regionally within Ontario (Tables 8 and 9) or interprovincially (Figure 10). Note that the rates in Figure 11 are age-standardized to the World Standard Population; they should not therefore be compared directly to those in Tables 8 and 9 and Figures 9 and 10, which were age-standardized to the Canadian 1991 population. Rates were generally high in Latin American populations (24.5-53.5 per 100,000) and in Asian populations in India and Thailand (20.2-38.9 per 100,000), being three or more times the rate in Ontario (8.4 per 100,000). Ontario incidence was comparable to or lower than that in the United States and most European countries. Finland had an exceptionally low incidence (3.6 per 100,000).

The explanations for the variation are likely to lie in differences in Pap test screening practices, sexual behaviour (in women and/or men), and socioeconomic status.

Figure 11. Age-standardized[1] incidence rates[2] for cervical cancer, by country/region, 1988-1992



[1] Standardized to the World Standard Population

[2] Uncorrected for hysterectomy

Cervical Cancer in Ontario 1971-1996

Morphology

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Morphologic patterns, by age group

Squamous cell carcinoma, including microinvasive squamous cell carcinoma, accounted for 68% of newly diagnosed cervical cancers at all ages in 1992-1996 (Table 10). Although this percentage was relatively constant across the age groupings shown, the proportion of microinvasive squamous cell carcinoma declined with increasing age while that of invasive squamous cell carcinoma rose. (Morphologic subgroups are described in Appendix D.)

An additional 18.7% of cases at all ages were adenocarcinoma and 4.3% adenosquamous carcinoma. The proportions were similar in all age groups.

About 2% of cervical cancers had other specific morphologies (e.g. sarcoma); this was consistent across age groups. A further 7.1% had no specified morphology; the proportion of tumours in this subgroup was highest in the oldest age group (10.6% for those aged 65+).

Table 10. Percentage distribution of morphologic types for cervical cancer in Ontario, by age group, 1992-1996

	All ages[1]		20-34		35-49		50-64		65+	
	#	%	#	%	#	%	#	%	#	%
Squamous cell carcinoma, excluding microinvasive	1,621	56.0	240	46.1	596	53.3	370	62.2	414	62.8
Microinvasive squamous cell carcinoma	348	12.0	102	19.6	161	14.4	46	7.7	39	5.9
Adenocarcinoma	543	18.7	103	19.8	237	21.2	101	17.0	102	15.5
Adenosquamous carcinoma	126	4.3	23	4.4	52	4.7	30	5.0	20	3.0
Other/specified morphology	54	1.9	12	2.3	18	1.6	10	1.7	14	2.1
Unspecified morphology	205	7.1	41	7.9	54	4.8	38	6.4	70	10.6
All morphologies[2]	**2,897**	**100.0**	**521**	**100.0**	**1,118**	**100.0**	**595**	**100.0**	**659**	**100.0**

[1] Totals across age groups may be less than the total for all ages because there are a few women under age 20 or of unknown age

[2] Percentages for some age groups do not add to exactly 100.0, due to rounding

Trends in incidence, by morphologic subgroup

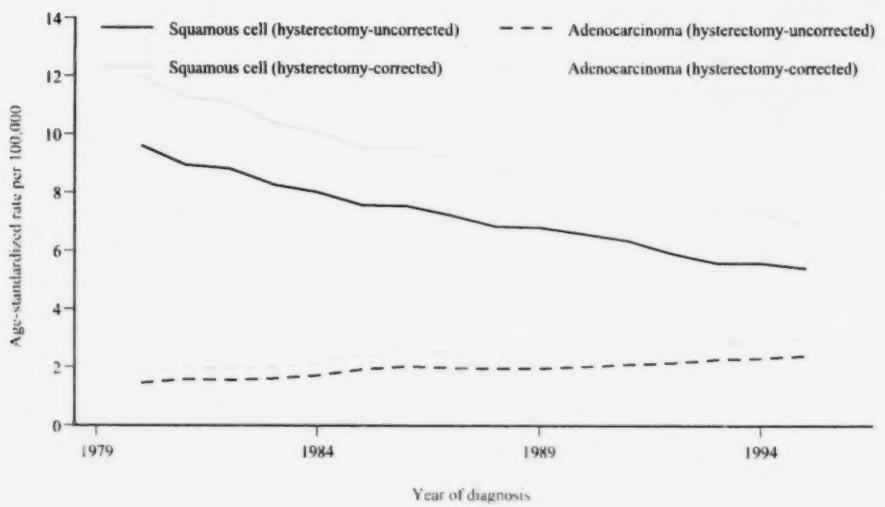
Trends over time for the major cervical cancer morphologic subgroups are shown in Figure 12 for the period 1979-1996, using both uncorrected and hysterectomy-corrected populations. Incidence declined steeply for squamous cell carcinoma (excluding microinvasive), from 12.0 per 100,000 (hysterectomy-corrected) in 1979-1981 to 7.0 in 1994-1996, a decline of 42%. The annual percentage decrease was 3.3%.

In contrast, although the incidence of adenocarcinoma (including adenosquamous carcinoma) was much lower, it rose steadily over the same period, from 1.8 per 100,000 (hysterectomy-corrected) in 1979-1981 to 3.0 in 1994-1996, an increase of 63%. The annual percentage increase was 3.4%. Adenocarcinoma and adenosquamous carcinoma appeared to be increasing at about the same rate.

The most likely explanation for the disparate trends in squamous cell cancer and adenocarcinoma relates to increasing rates of infection with oncogenic types of human papilloma virus (HPV), particularly in younger women (Vizcaino et al. 1998). This would be expected to result in increased incidence of both forms of the disease. However, Pap test screening may have prevented the incidence of squamous cell carcinoma (but not adenocarcinoma) from rising because screening, as historically practised in Ontario, is more effective at detecting squamous cell carcinoma.

Although the incidence of cervical cancer of unspecified morphologic type has decreased over the time period, it is unlikely that this completely explains the increasing incidence of adenocarcinoma. However, increased awareness of and proficiency at detecting adenocarcinoma and its precursors on Pap tests may have accounted for part of the rise in adenocarcinoma incidence.

Figure 12. Age-standardized incidence rates (3-year moving averages) for cervical cancer in Ontario, by morphologic subgroup,[1] 1979-1996



[1] Squamous cell carcinoma excludes microinvasive. Adenocarcinoma includes adenosquamous carcinoma

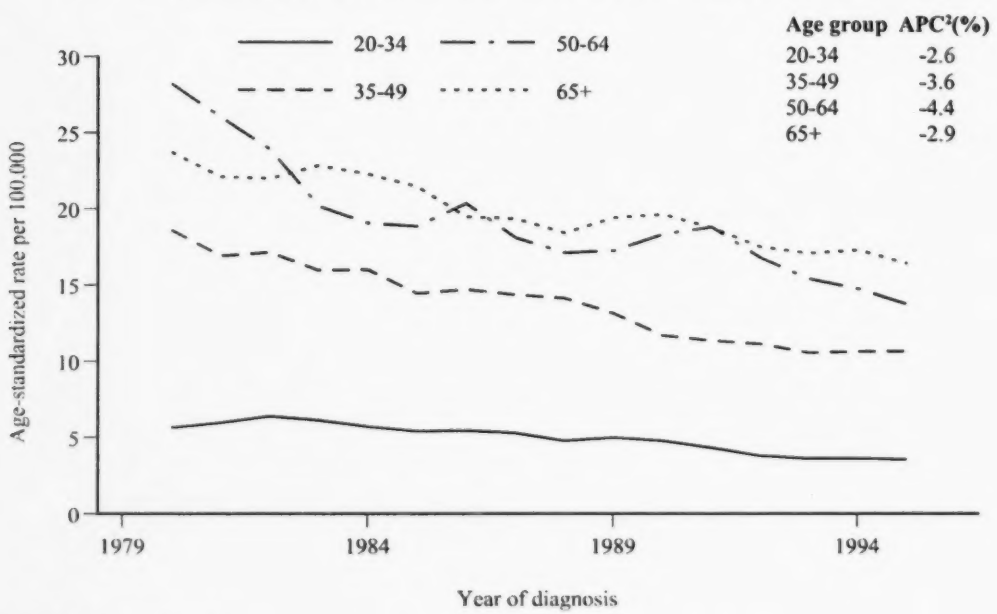
Trends in incidence for morphologic subgroups, by age

Squamous cell carcinoma (excluding microinvasive)

Figure 13 shows hysterectomy-corrected incidence rates for squamous cell carcinoma (excluding microinvasive) according to age at diagnosis. The incidence was lowest for those aged 20-34 and highest for those aged 50-64 and 65+.

Although the incidence decreased over time in every age group, the rate of decline was least for the youngest age group at 2.6% per year. Compared to the trend for all morphologies combined (Figure 7 and Table 6), where the annual percentage decrease in incidence for those aged 20-34 was only 0.9% during the time period 1975 to 1996, this represents a substantial annual decline. Annual rates of decrease for the other age groups were likewise greater for squamous cell carcinoma than for all cervical cancer, over comparable years of diagnosis.

Figure 13. Age-standardized hysterectomy-corrected incidence rates (3-year moving averages) for squamous cell carcinoma of the cervix[1] in Ontario, by age group, 1979-1996



[1] Excludes microinvasive

[2] APC = annual percentage change

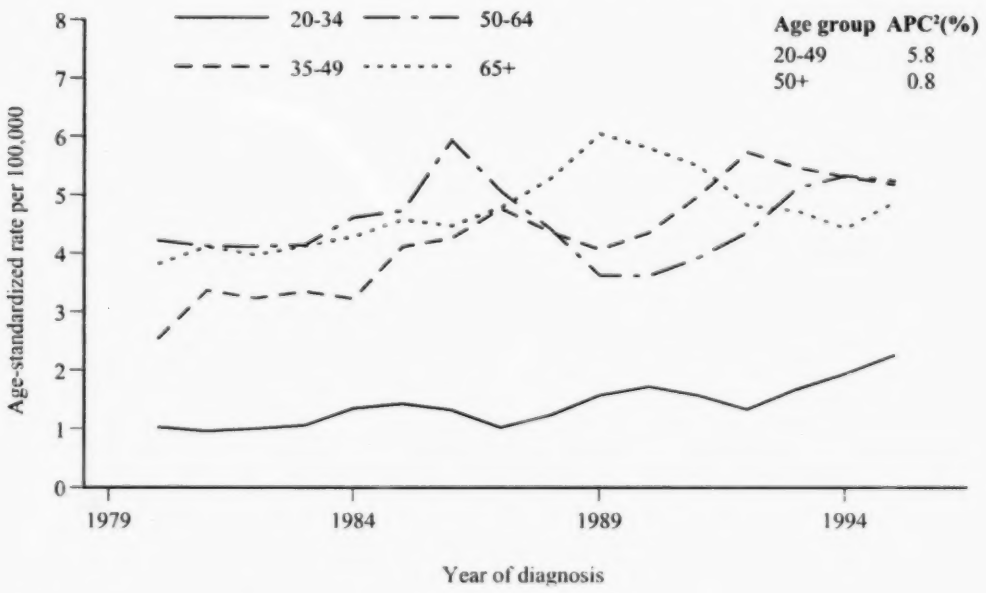
Adenocarcinoma (including adenosquamous carcinoma)

The incidence of adenocarcinoma (including adenosquamous carcinoma), corrected for hysterectomy, was lowest for the youngest age group (20-34) and roughly similar for the other three age groups (Figure 14).

In contrast to the downward trends in every age group for squamous cell carcinoma, rates of adenocarcinoma have more than doubled in women aged 20-34 and 35-49, with an annual percentage increase of 5.8%. (The two youngest and the two oldest age groups were combined for estimating trend due to the small numbers in the groups separately.) Trends in the older age groups were less pronounced, with a small annual increase of 0.8%.

The strong upward trend in young women is probably the result of a birth cohort effect (Vizcaino et al. 1998), with women born more recently (and hence younger at diagnosis) at higher risk than earlier-born cohorts. This is generally attributed to increased rates of infection with oncogenic types of HPV, beginning with women who were part of the "sexual revolution" of the 1960s and 1970s (Vizcaino et al. 1998). Increasing use of oral contraceptives may also have played a role in the rising incidence in young women.

Figure 14. Age-standardized hysterectomy-corrected incidence rates (3-year moving averages) for adenocarcinoma of the cervix[1] in Ontario, by age group, 1979-1996



[1] Includes adenosquamous carcinoma

[2] APC = annual percentage change

Cervical Cancer in Ontario
1971-1996

Survival

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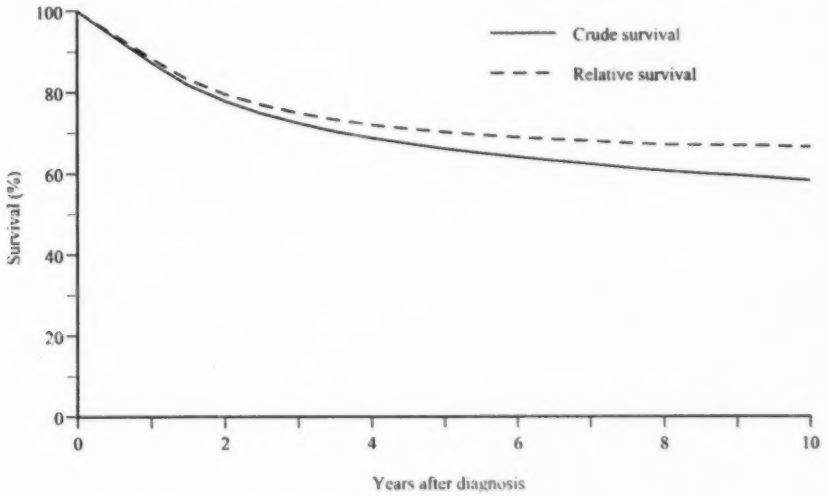
Crude and relative survival

The 1-year relative survival after diagnosis of cervical cancer was 88.4% and the 5-year relative survival was 70.3% (Figure 15). Relative survival declined only slightly after 5 years to about 67% at 10 years.

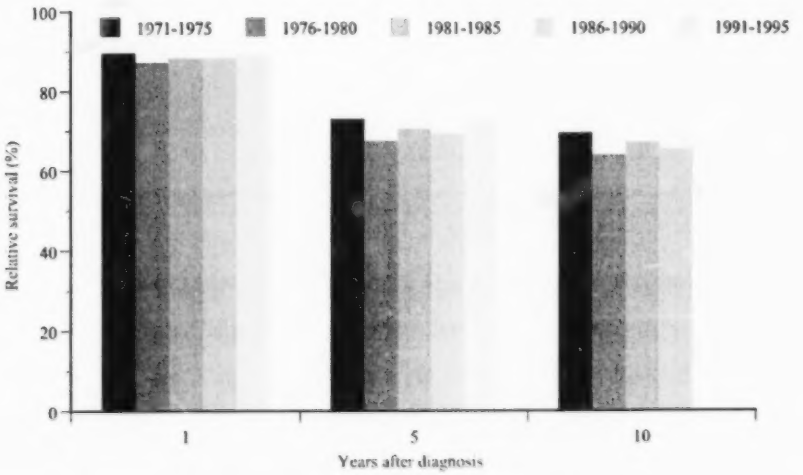
Figure 15. Crude and relative survival for cervical cancer in Ontario, 1971-1996



Relative survival, by period of diagnosis

Figure 16 presents 1-, 5- and 10-year relative survival rates for five periods of diagnosis: 1971-1975 through 1991-1995. Relative survival remained constant over these periods. It is difficult to interpret these results without information about stage of disease at diagnosis.

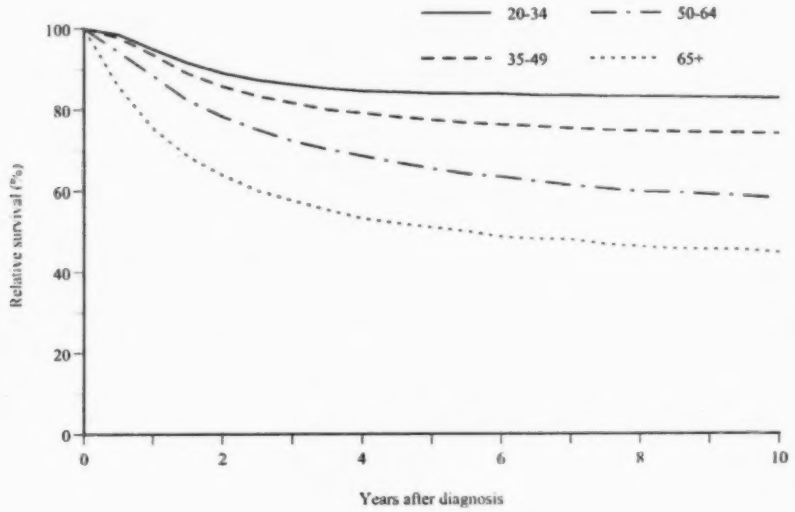
Figure 16. Relative survival for cervical cancer in Ontario, by period of diagnosis, 1971-1995



Relative survival, by age group

Survival varied considerably with age at diagnosis, with 5-year relative survival rates ranging from 83.9% in those diagnosed at age 20-34 to only 50.9% in those aged 65+ at diagnosis (Figure 17).

Figure 17. Relative survival for cervical cancer in Ontario, by age group, 1971-1996

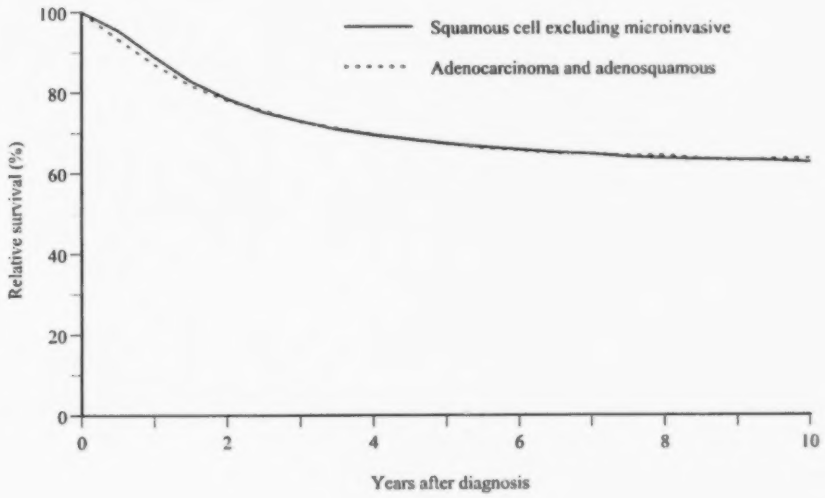


Relative survival, by morphologic subgroup

Relative survival for squamous cell carcinoma (excluding microinvasive) and for adenocarcinoma and adenosquamous carcinoma combined is presented in Figure 18. Survival for the two morphologic subgroups was virtually identical, with a 5-year relative survival rate of 67.4% for each. This was somewhat lower than the overall 5-year relative survival rate of 70.3% (Figure 16), presumably because the latter included microinvasive lesions, which would be expected to have very good survival.

The similarity in 5-year relative survival rates by morphologic subgroup hides some apparent differences by age at diagnosis: 5-year survival rates for adenocarcinoma/adenosquamous carcinoma were higher than those for squamous cell carcinoma (excluding microinvasive) at younger ages (significantly so for those aged 35-49 at diagnosis) and lower at older ages (significantly so for those aged 65+).

Figure 18. Relative survival for cervical cancer in Ontario, by morphologic subgroup, 1979-1996



Cervical Cancer in Ontario 1971-1996

Material and Methods/References /Appendices

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Data sources

New cases of cancer

The Ontario Cancer Registry (OCR), operated by Cancer Care Ontario (CCO), registers all newly diagnosed cases of cancer (invasive neoplasms), except non-melanoma skin cancers. While cancer reporting is not a legal requirement in Ontario, the Cancer Act provides a legal mandate for this undertaking and offers legal protection for physicians, dentists and health care agencies which report information on cancer cases.

The process of cancer registration in Ontario is passive, relying almost completely on records collected for other purposes. Since 1977, the OCR has relied on the same four major data sources: hospital discharge summaries which include a diagnosis of cancer; pathology reports with any mention of cancer; records of patients referred to CCO's eight Regional Cancer Centres (RCCs) or the Princess Margaret Hospital (PMH) (now part of the University Health Network), the specialized institutions treating cancer patients in Ontario; and death certificates with cancer as the underlying cause of death.

All records except pathology reports are coded at the source and provided to the OCR in machine-readable form. Paper copies of pathology reports are sent to the OCR by all hospital and private pathology laboratories and are coded and key-entered by OCR staff. Since 1991, the OCR has also received day surgery summaries which include a diagnosis of cancer. The OCR receives about 400,000 records from these multiple sources each year. The OCR is highly automated, relying heavily on automated edit-checking, computerized probabilistic record linkage and automated rule-based systems for summarizing patient and tumour information. Further details about the operation are available in recent monographs (Holowaty et al. 1995; Marrett et al. 1995; McLaughlin et al. 1995).

Quality of data for new cases of cancer

Microscopic examination of tissue or cells is the definitive diagnostic test for cancer. During the period 1971-1996, 10.6% of cervical cancers were not microscopically verified in the OCR. This proportion decreased to under 5% (4.2%) for the more recent interval 1979-1996, largely because of more complete reporting from pathology laboratories. This rate of non-microscopic confirmation is still somewhat above that reported by established active registries; for instance, the American SEER (Surveillance, Epidemiology and End Results Program) registries report a rate of 3%.

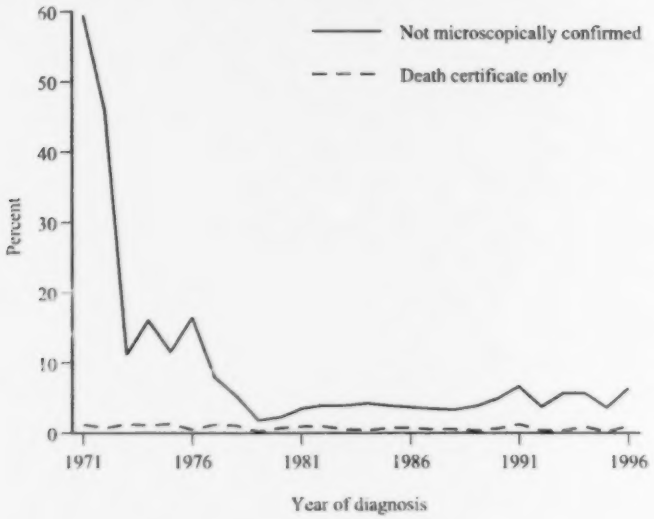
Another parameter of data quality is the percentage of cases for which a death certificate is the only source of information supporting a diagnosis of cervical cancer. Only 0.8% of cervical cancers registered from 1971-1996 were registered from death certificates only. Figure 19 shows the temporal trends in data quality indicators for cervical cancer.

Because the management of cervical cancer almost always requires contact with institutions that comprise two or more of the OCR's major reporting sources, it is likely that reporting is almost complete. During the 1971-1996 time period, only 3.3% of cervical cancer cases registered in the OCR were identified by a single source, with 0.8% and 2.5% of cases, respectively, being identified by death certificates and hospitalization records only.

Deaths from cancer

Mortality data in the OCR are largely derived from the Office of the Registrar General of Ontario, where death certificate information is collected and coded. Mortality rates are estimated from the

Figure 19. Temporal trends in data quality indicators



reported underlying cause of death, coded according to the International Classification of Diseases - Ninth Revision (ICD-9) (WHO 1977), among persons residing in Ontario at the time of death.

Population data

Rates were calculated using annual mid-year estimated resident populations of females by 5-year age group. These estimates are based on the National Population Census, conducted every five years, and are corrected for census undercounts. Populations for both Ontario and its census divisions were provided by Statistics Canada (Statistics Canada 1997). Populations for CCO Regions (CCORs) and Public Health Units (PHUs) were determined by adding the populations for all census divisions that comprise each Region or Unit (see Appendices B and C).

The age distribution of the 1991 Canadian population, adjusted for census undercount, was used to calculate most of the age-standardized rates appearing in this monograph (see Appendix A). For international comparisons, the World Standard Population was used to calculate the age-standardized rates (see Appendix A).

Hysterectomy correction of population at risk for cervical cancer

Ontario women at risk for cervical cancer are those who have not had a hysterectomy which includes removal of the ectocervix. Some incidence and mortality trends are shown in this monograph in two ways. Rates based on the total female population of the province allow for comparison with other regions in Canada and the world. Rates providing a more accurate assessment for Ontario as a whole are based on total women minus the number estimated to have had a prior hysterectomy. Adjusted population counts were derived by multiplying the cumulative probability of not having had a hysterectomy for a woman of a given age by the total number of women in Ontario of that age in each year (Holowaty 1996).

Hysterectomy data were provided by Statistics Canada for 1971-1976 and by the Hospital Medical Records Institute (HMRI) / Canadian Institute for Health Information (CIHI) for 1980-1996. For

1977-1979, hysterectomy counts were imputed from the available data for six years prior to and three years following these three years (P. Holowaty, personal communication).

National and international data

Health Canada provided incidence rates of cervical cancer by province using data from the Canadian Cancer Registry at Statistics Canada (R. Semenciw, personal communication). The incidence rates of cervical cancer around the world were recently published by the International Agency for Research on Cancer (IARC) (Parkin 1997). This monograph covers the period 1988-1992 for most reporting registries. For comparison with Ontario incidence data, countries were selected to represent different continents, but also had to meet all of the data quality requirements of the IARC publication. No areas of Africa qualified for this comparison. Registries in Oceania were excluded because their cervical cancer rates were similar to those in North America.

Incidence and mortality data

Cancer site

A cancer is generally coded according to the body site at which it occurs. In the OCR, the primary site of cancer/cancer cause of death has been coded according to ICD-9 (WHO 1977). The ICD-9 code for invasive cancer of the cervix uteri is 180. Although this code has a fourth digit which theoretically indicates the more specific site of the cancer within the cervix (180.0 for endocervix and 180.1 for ectocervix), this digit is usually recorded in the OCR as a '9', which means that there was no subsite specified. Therefore, data have been presented only for site 180 as a whole.

Morphology

The microscopic morphology or histopathology of tumours concerns the appearance of cancerous cells, tissues and organs under the light microscope. The morphologic type of a cancer may be a prognostic factor; additionally, it may be important for treatment decisions. It may also be important in epidemiologic studies of cancer etiology. Cancers of different morphologic types that occur in the same anatomic site often have different etiologies, incidences and prognoses.

The morphologic data presented in this monograph have been coded according to the First Edition of the International Classification of Diseases for Oncology (ICD-O) (WHO 1976; Percy et al. 1990). The morphology code in ICD-O consists of five digits. The first four digits describe the morphologic type, and the fifth digit describes the behaviour. The OCR registers only malignant neoplasms; that is, those with a behaviour code of 3.

As the total number of morphologic types recognized in ICD-O approaches 500, grouping of the various types is necessary. Appendix D shows the grouping scheme employed for this monograph, a variant of Parkin and co-authors' groups for comparative studies (Parkin et al. 1998). In Table 10 we show adenosquamous carcinoma separately, although this morphologic type was too infrequent to treat it as a separate category for analysis of time trends. In including it with adenocarcinoma we have followed the most usual practice, although some published analyses include it with squamous cell carcinoma (Platz and Benda 1995; Parkin et al. 1998; Berg 1996).

Squamous cell carcinomas designated "microinvasive" in the OCR are included as a separate line in Table 10 but have been excluded from the morphology-specific analyses in this monograph. Coding of this term by OCR staff may not have been consistent across the years, the spread of its use and its accepted definition among Ontario pathologists is uncertain, and the medical literature suggests that

differing definitions have been used (Benedet and Anderson 1996; Lecuru et al. 1997). Cases in the OCR possibly represent at least some that would previously have been classified as in-situ cancers and excluded, so that their inclusion would give a misleading sense of trends in incidence, mortality and survival.

Spread of cancer at diagnosis (stage)

The OCR does not routinely collect information about the stage of cancer at diagnosis, primarily because this information is not captured by all reporting sources. Stage distribution from a Canadian population has been reported for 241 of 246 Alberta women diagnosed with invasive cancer during 1990 and 1991 (Stuart et al. 1997). Fifteen percent of women had Stage IA disease, 51.6% had Stage IB, 18.7% had Stage II and 12.6% had Stages III and IV. The Ontario distribution, although unknown, may be similar; the 12% "microinvasive" in Table 10 is close to the 15% in Alberta designated Stage IA, which may mainly represent microinvasive disease.

Time periods

Incidence, mortality and survival trends are presented in this monograph for the period 1971-1996. While the OCR actually begins in 1964, population estimates adjusted for census undercount are only available since 1971; 1996 is the most recent year for which there is complete reporting.

The most recent 5-year time period, 1992-1996, was used to estimate the burden of cancer and to describe selected characteristics of tumours or cases. This 5-year aggregate stabilizes estimates of infrequent events (diagnoses at younger ages, for example) while providing the most current information.

More detailed analyses by morphologic subgroup are focused on the period 1979-1996, because of the appreciable improvement in the rates of microscopic confirmation between 1971 and 1979 (Figure 19). Other periods are used occasionally because of availability; for example, data from other provinces of Canada are for 1991-1995, because that is the most recent period available. The most recently published international data are for 1988-1992.

Residence at diagnosis and death

The geographic variation in incidence and mortality in cervical cancer in Ontario over the period 1992-1996 is described in terms of Cancer Care Ontario Regions (CCORs) and Public Health Units (PHUs), which are aggregations of census divisions (see Appendices B and C). Census division of residence at the time of diagnosis comes primarily from hospital records in the OCR. All but 1.8% of cases of cervical cancer in 1992-1996 have a census division of residence recorded. Because of the small percentage of cases with missing residence, all incidence rates calculated for the purpose of comparing the CCORs or PHUs to the province exclude cases with missing residence. Census division of residence at time of death comes from death certificates in the OCR. Mortality rates for CCOR comparisons were also calculated with missing residence excluded, since 0.4% of records of cervical cancer deaths for the 1992-1996 time period did not report a valid census division of residence.

The eight CCORs cover the entire province, with populations ranging from 5.3 million in the largest (Central East CCOR) to 367,000 in the smallest (South CCOR) (Statistics Canada 1997). Within each CCOR is situated one of CCO's Regional Cancer Centres (RCCs). In addition, Princess Margaret Hospital (PMH) is located within the Central East CCOR. Maps describing CCOR boundaries and census division components are shown in Appendix B.

Appendix C contains a map showing Ontario PHUs and a table showing corresponding census divisions as used for PHU analysis. It should be noted that actual PHU boundaries are not always equivalent to those for the grouped census divisions as used herein. The discrepancy is greatest in northern Ontario. The following PHUs do not correspond exactly to groups of census divisions: Algoma, Muskoka-Parry Sound, North Bay and District, Northwestern, Porcupine, Renfrew, Sudbury and District, Thunder Bay, and Timiskaming.

Statistical methods

Age-specific rates

Age-specific rates were calculated in 5-year age groups by dividing the number of cases or deaths by the Ontario female population in the same age group for the same calendar period. Age-specific rates are expressed per 100,000 person-years.

Age-standardized rates

To compare incidence and mortality rates between populations which have different age structures, age-standardized rates were calculated. The age-standardized rate is a weighted average of the age-specific rates, using a standard population age distribution. The standardized rates reflect the incidence and mortality that would be expected if the population of interest had an age structure identical to the standard population. The 1991 Canadian population, adjusted for census undercount (Appendix A), was used as the standard throughout most of this monograph. However, in comparisons between Ontario's rate and those of other parts of the world, the World Standard Population was used (see Appendix A). Age-standardized rates are expressed per 100,000 person-years.

Time trends

The annual numbers of incident cases and deaths were plotted to describe the total burden of cervical cancer for the period 1971-1996. To illustrate time trends, 3-year moving averages of age-standardized incidence and morality rates were plotted, for all ages and by age group. Three-year moving averages were used to smooth out annual fluctuations, which can occur when there are small numbers of cases. Trends by morphologic subgroup were plotted from 1979 to 1996, again using 3-year moving averages.

In order to estimate the annual percentage change (APC) (Esteve et al. 1994), the logarithm of the annual rate was modelled as a function of year of diagnosis or death using weighted linear regression and SAS® PROCs REG and GLM (SAS 1997). First, the entire time period was modeled, allowing the inclusion of a quadratic year term if necessary. If the quadratic term was found to be significant or if the model fit was poor, a change-point analysis was undertaken to determine the year at which the rate of annual increase or decrease changed markedly (Shaban 1980). In this second step, two lines were fit to the data (one prior to the change point and one after) to try to improve the model; the increase in the percentage of variation explained by the model (R^2) was used to select the best two-line model.

The APC estimates are reported either for the entire time period or for two time periods, depending on the results of the change-point analysis.

Rate ratios

The comparison of incidence or mortality rates in two populations (or subgroups), as a ratio of these rates, is termed a rate ratio (RR) or relative rate. In this monograph, this technique was employed for comparison of the rates of cervical cancer for each CCOR or PHU to that of the province as a whole. The rates for each population were age-standardized, using the 1991 Canadian population, adjusted for census undercount (Appendix A), as the standard. A rate ratio in excess of 1.0 for regional comparisons, for example, means that the region has a higher rate than Ontario as a whole.

Confidence intervals

A confidence interval (CI) indicates the range of values for a parameter of interest (e.g. a rate ratio) which has a specified probability of including the true value. Thus, the 95% CI for a RR represents the interval which has a 95% chance of covering the true value of the RR. The 95% CI for each incidence and mortality RR comparing a regional rate to the provincial rate is calculated using the approximate bootstrap confidence interval method (Swift 1995).

When the 95% CI includes 1.0, the RR is considered not to differ significantly from 1.0 (i.e. the rate for the region does not differ significantly from that for the province), and the difference between the RR and 1.0 is ascribed to chance variation. If the interval does not include 1.0, the RR is deemed to be statistically significantly different from 1.0. A RR is declared to be significantly low if the upper limit of the CI is less than 1.0 and significantly high if the lower limit of the CI is greater than 1.0. Due to rounding, a RR may occasionally be declared to differ significantly from 1.0 when one of the end points of the CI is 1.0.

Survival

Cases with a first primary diagnosis of cervical cancer between 1971 and 1996 were used in the survival analyses for all cases and by age group; the time period 1979-1996 was used for the analyses by morphologic subgroup. Cases were followed for deaths occurring through December 31, 1997 (as recorded in the OCR). The outcome of interest was all-cause mortality. If no death information was available, cases were assumed to be alive through December 31, 1997.

Life table methods using 6-month intervals were used to calculate crude survival rates for up to 10 years (Namboodiri and Suchindran 1987). SAS® PROC LIFETEST was used for these analyses (SAS 1997). Although the crude survival rate is actually a proportion, in standard terminology it is referred to as a "rate". The relative survival rate is a measure of the influence of cervical cancer on normal life expectancy, because it is obtained by adjusting the crude survival for the average life expectancy of the general population of the same age as women diagnosed with cervical cancer. (A more detailed description can be found in McLaughlin et al. 1995.) Since it is generally acknowledged that cause of death information on death certificates is often not accurate enough to determine whether an individual died from his or her original cancer, the relative survival rate is the preferred method for reporting survival from cancer registry data. A FORTRAN program developed by Hakulinen et al. (Hakulinen and Abeywickrama 1985) was used for the relative survival analyses.

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Appendices

Appendix A. World and Canadian standard populations and Ontario 1996 population

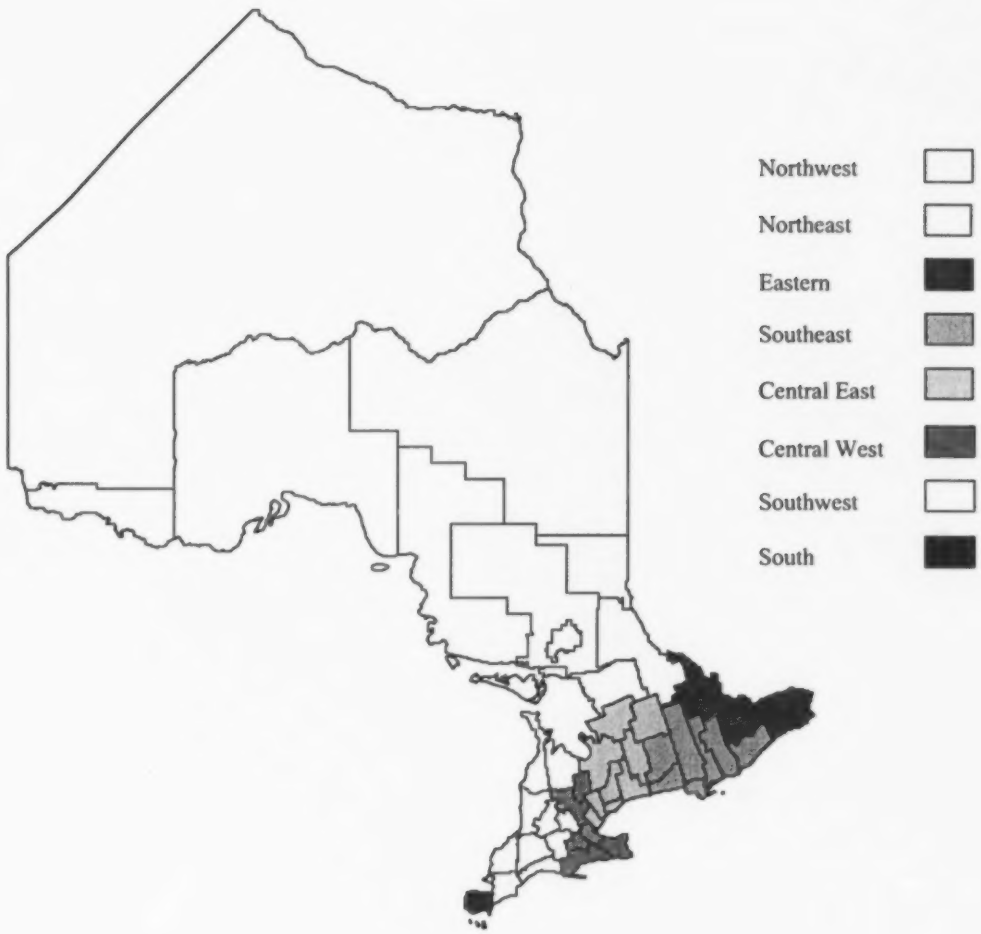
Age	World Standard Population[1]	Canadian 1991 Population[2]	Ontario 1996 Population[3]
0-4	12,000	6946.4	747,717
5-9	10,000	6945.4	761,924
10-14	9,000	6803.4	746,766
15-19	9,000	6849.5	721,674
20-24	8,000	7501.6	757,574
25-29	8,000	8994.4	858,206
30-34	6,000	9240.0	1,023,410
35-39	6,000	8338.8	996,706
40-44	6,000	7606.3	874,646
45-49	6,000	5953.6	804,424
50-54	5,000	4764.9	616,522
55-59	4,000	4404.1	503,292
60-64	4,000	4232.6	462,390
65-69	3,000	3857.0	433,907
70-74	2,000	2965.9	378,250
75-79	1,000	2212.7	261,584
80-84	500	1359.5	170,896
85+	500	1023.7	132,537
Total	**100,000**	**100,000**	**11,252,425**

[1] Parkin et al. 1997

[2] Statistics Canada 1994 . Represented for convenience as the proportional distribution ac ross age groups, rather than as actual population c ounts

[3] Statistics Canada 1997

Appendix B. Cancer Care Ontario Regions (CCORs)



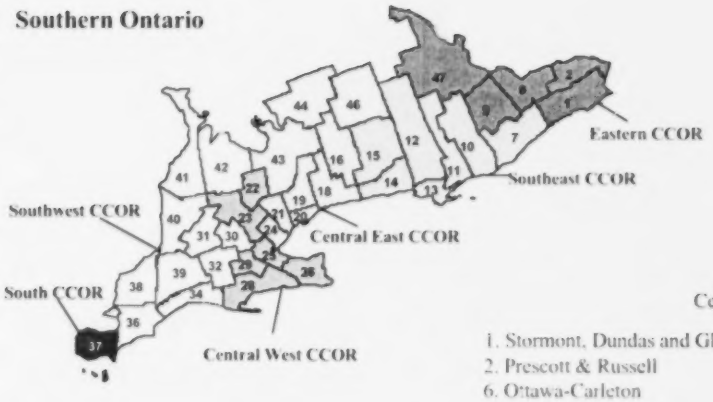
Appendix B (continued). Cancer Care Ontario Regions (CCORs) showing census divisions

Northern Ontario

Census Divisions

48. Nippissing
49. Parry Sound
48. Nippissing
51. Manitoulin Island
52. Sudbury District
53. Sudbury R.M.
54. Timiskaming
56. Cochrane
57. Algoma
58. Thunder Bay
59. Rainy River
60. Kenora

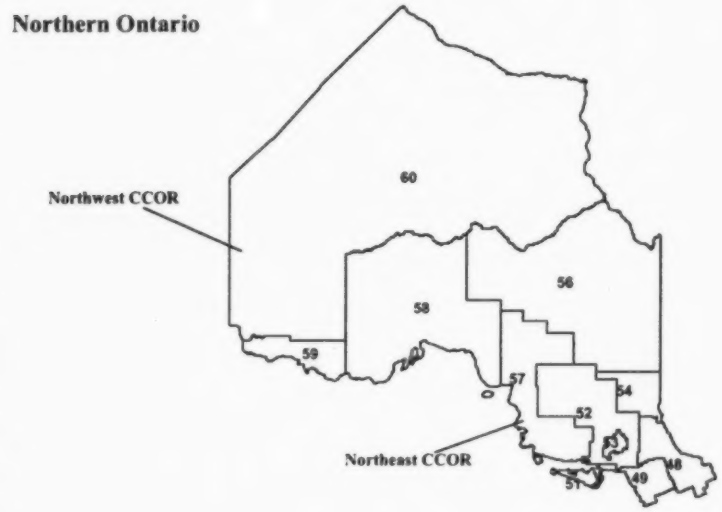
Southern Ontario



Census Divisions

1. Stormont, Dundas and Glengarry
2. Prescott & Russell
6. Ottawa-Carleton
7. Leeds & Grenville
9. Lanark
10. Frontenac
11. Lennox & Addington
12. Hastings
13. Prince Edward
14. Northumberland
15. Peterborough
16. Victoria
18. Durham
19. York
20. Toronto
21. Peel
22. Dufferin
23. Wellington
24. Halton
25. Hamilton-Wentworth
26. Niagara
28. Haldimand Norfolk
29. Brant
30. Waterloo
31. Perth
32. Oxford
34. Elgin
36. Kent
37. Essex
38. Lambton
39. Middlesex
40. Huron
41. Bruce
42. Grey
43. Simcoe
44. Muskoka
46. Haliburton
47. Renfrew

Appendix B (continued). Cancer Care Ontario Regions (CCORs) showing census divisions



Census Divisions

48. Nippissing
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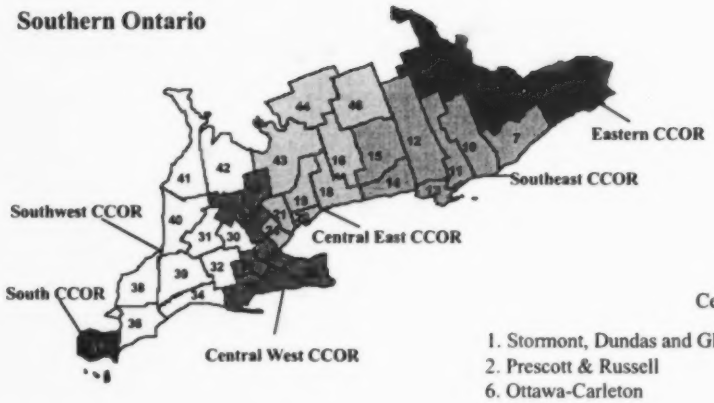
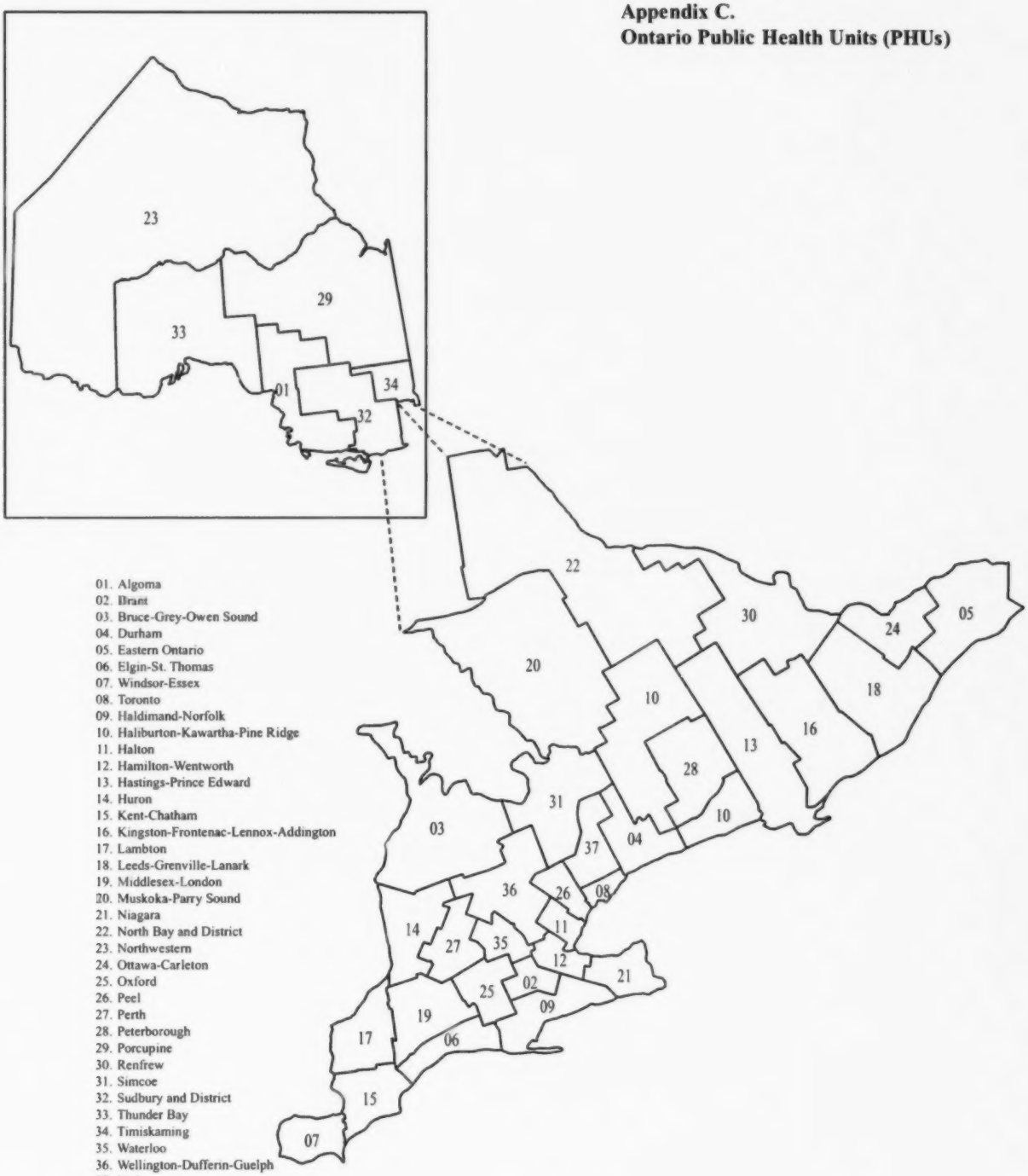
52. Sudbury District
53. Sudbury R.M.
54. Timiskaming
56. Cochrane
57. Algoma
58. Thunder Bay
59. Rainy River
60. Kenora



Census Divisions

1. Stormont, Dundas and Glengarry
2. Prescott & Russell
6. Ottawa-Carleton
7. Leeds & Grenville
9. Lanark
10. Frontenac
11. Lennox & Addington
12. Hastings
13. Prince Edward
14. Northumberland
15. Peterborough
16. Victoria
18. Durham
19. York
20. Toronto
21. Peel
22. Dufferin
23. Wellington
24. Halton
25. Hamilton-Wentworth
26. Niagara
28. Haldimand Norfolk
29. Brant
30. Waterloo
31. Perth
32. Oxford
34. Elgin
36. Kent
37. Essex
38. Lambton
39. Middlesex
40. Huron
41. Bruce
42. Grey
43. Simcoe
44. Muskoka
46. Haliburton
47. Renfrew

Appendix C.
Ontario Public Health Units (PHUs)



01. Algoma
02. Brant
03. Bruce-Grey-Owen Sound
04. Durham
05. Eastern Ontario
06. Elgin-St. Thomas
07. Windsor-Essex
08. Toronto
09. Haldimand-Norfolk
10. Haliburton-Kawartha-Pine Ridge
11. Halton
12. Hamilton-Wentworth
13. Hastings-Prince Edward
14. Huron
15. Kent-Chatham
16. Kingston-Frontenac-Lennox-Addington
17. Lambton
18. Leeds-Grenville-Lanark
19. Middlesex-London
20. Muskoka-Parry Sound
21. Niagara
22. North Bay and District
23. Northwestern
24. Ottawa-Carleton
25. Oxford
26. Peel
27. Perth
28. Peterborough
29. Porcupine
30. Renfrew
31. Simcoe
32. Sudbury and District
33. Thunder Bay
34. Timiskaming
35. Waterloo
36. Wellington-Dufferin-Guelph
37. York

Appendix C (continued). Ontario Public Health Units (PHUs) showing corresponding census divisions

Public Health Unit	Census divisions
Algoma	Algoma
Brant	Brant
Bruce-Grey-Owen Sound	Bruce
	Grey
Durham	Durham
Eastern Ontario	Prescott and Russell
	Stormont, Dundas and Glengarry
Elgin-St. Thomas	Elgin
Haldimand-Norfolk	Haldimand-Norfolk
Haliburton-Kawartha-Pine Ridge	Haliburton
	Northumberland
	Victoria
Halton	Halton
Hamilton-Wentworth	Hamilton-Wentworth
Hastings-Prince Edward	Hastings
	Prince Edward
Huron	Huron
Kent-Chatham	Kent
Kingston-Frontenac-Lennox-Addington	Frontenac
	Lennox and Addington
Lambton	Lambton
Leeds-Grenville-Lanark	Lanark
	Leeds and Grenville
Middlesex-London	Middlesex
Muskoka-Parry Sound	Muskoka
	Parry Sound
Niagara	Niagara
North Bay and District	Nipissing
Northwestern	Kenora
	Rainy River
Ottawa-Carleton	Ottawa-Carleton
Oxford	Oxford
Peel	Peel
Perth	Perth
Peterborough	Peterborough
Porcupine	Cochrane
Renfrew	Renfrew
Simcoe	Simcoe
Sudbury	Manitoulin Island
	Sudbury District
	Sudbury R.M.
Thunder Bay	Thunder Bay
Timiskaming	Timiskaming
Toronto	Toronto
Waterloo	Waterloo
Wellington-Dufferin-Guelph	Dufferin
	Wellington
Windsor-Essex	Essex
York	York

Appendix D. Description of morphologic subgroups for cancer of the cervix

Subgroup (modified from Parkin et al. 1998)	**ICD-O morphology code**[2] (WHO 1976)
Squamous cell carcinoma, excluding microinvasive	8051-8075
Microinvasive squamous cell carcinoma	8076
Adenocarcinoma	8050, 8140-8510[1]
Adenosquamous carcinoma	8560, 8570
Unspecified morphology	8000-8034, 9990
Other specified morphology	All other codes

[1] Not all codes in this range apply to the cervix

[2] International Classification of Diseases for Oncology